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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,476	09/30/2003	Robert B. DuBridge	181 US UT01	7526

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PDL BIOPHARMA, INC.
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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	

MAIL DATE	DELIVERY MODE
12/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/676,476	DUBRIDGE, ROBERT B.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *89-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/17/2007 has been entered.

Receipt is acknowledged of an amendment, filed 9/17/2007, in which claims 1-88 were canceled, and claims 89-103 were newly added. Currently, claims 89-103 are pending.

Any rejection of record in the previous office actions not addressed herein is withdrawn.

Election/Restrictions

Applicant elected Group I without traverse in the reply filed 3/18/2005. Applicant confirmed the provisional election of Flp recombinase as the species of recombinase in the reply filed 11/29/2005. All pending claims are readable upon the elected invention.

Currently, claims 89-103 are under consideration.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re*

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 89-92 and 95-103 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3-6, 8, 9, 11, 13, 15 and 16 of copending Application No. 11/509,177 (hereinafter the '177 application). This is a new rejection.

Although the conflicting claims are not identical, they are not patentably distinct from each other. Conflicting claim 15 is drawn to the same cellular expression system as instant claim 89; however, conflicting claim 15 does not specifically recite the structural characteristics of the second integration cassette and second target cassette. It would be obvious to include a second integration cassette with the same structural characteristics as the first integration cassette and a second target cassette with the same structural characteristics as the second target cassette, as evidenced by conflicting claim 13. Thus, instant claims 89, 95 and 97 are obvious variants of conflicting claims 15 and 13. Instant claim 92 is an obvious variant of conflicting claim 16 in that both claims require the protein complex to be an antibody. Other obvious variants of conflicting claim 15, include embodiments where the rec element is included in the target cassette (claim 3), where the scorable reporter gene is a membrane-bound protein selected from

CD8 or CD4 (claim 4), where the host cell is selected from the group consisting of mammalian cells, yeast cell, or bacterial cells (claim 5), where the integration cassette further comprises a polycistronic element (claim 6), where the integration cassette further comprises a tag (claim 8), where the target element comprises a target gene and selectable marker gene (claim 9), and where the target cassette further comprises a tag (claim 11). Accordingly, instant claims 96, 90 & 91, 103, 99, 98, 101 & 102 and 100 are obvious variants of conflicting claims 3, 4, 5, 6, 8, 9, and 11, respectively.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments - 35 USC § 112

The rejection of claims 85-88 under 35 U.S.C. 112, second paragraph, is moot in view of Applicant's cancellation of the claims in the reply filed 9/17/2007.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 89, 90, 92-95 and 97-103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheo et al (US Patent Application Publication No. 2002/0007051, cited in a

prior action; see the entire reference) in view of Seibler et al (Biochemistry, Vol. 36, pages 1740-1747, 1997, cited in a prior action; see the entire reference). This is a new rejection necessitated by the addition of new claims 89, 90, 92-95 and 97-103 in the amendment filed 9/17/2007.

Regarding claims 89 and 95, Cheo et al teach an integration cassette (e.g. starting molecule or destination vector) comprising two recombination sites flanking promoters, selectable markers, and tags such histidine tags or green fluorescent protein (e.g. paragraphs [0045], [0050], [0147], [0148], [208] and [0488]; Figure 6). Cheo et al define the term "selectable marker" to mean a nucleic acid segment that allows one to select for or against a molecule or cell that contains it, often under particular conditions, including nucleic acid segments that encode products which can be readily identified (e.g., phenotypic markers such as P-galactosidase, green fluorescent protein (GFP), yellow fluorescent protein (YFP), red fluorescent protein (RFP), cyan fluorescent protein (CFP), and cell surface proteins (paragraph [0258]). Further, Cheo et al teach the addition of regions that allow integration into eukaryotic chromosomes (e.g. transposable elements) (e.g. paragraph [0327]). As a general rule, the insertion of transposons into target DNA is a random event (e.g. paragraph [0010]). Cheo et al teach a first target cassette comprising a polynucleotide to be substituted into the integration cassette flanked by two recombination sites (e.g. paragraphs [0045] and [0075]). Regarding the recombination sites and additional vectors, Cheo et al teach the following:

> In another specific aspect, the invention provides a method of cloning comprising providing at least a first nucleic acid molecule comprising at least a first and a second recombination site and at least a second nucleic acid molecule comprising at least a third and a fourth recombination site, wherein none of the first, second, third or fourth recombination sites is capable of recombining with any of the other sites, providing one or more vectors (e.g., two, three, four, five, seven, ten, twelve, etc.), comprising at least a fifth, sixth, seventh and eighth recombination site, wherein each of the fifth, sixth, seventh and eighth

> recombination sites are capable of recombining with one of the first, second, third or fourth recombination site, and conducting a recombination reaction such that at least said first and second molecules are recombined into said vectors. See paragraph [0154].

See also Figures 6 and 7 and paragraph [0075], for example. Further, Cheo et al teach a recombinase activity capable of recognizing the recombinase recognition sites of the second integration cassette and second target cassette (e.g. paragraphs [0055], [0196], [0253] and [0295]). Cheo et al teach the use of the Flp recombinase protein to catalyze recombination between Frt sites (e.g. paragraphs [0047], [0048], [0055] and [0253]). Cheo et al teach the system with target cassettes each containing a nucleic acid molecule encoding a subunit of a multi-subunit complex such as an enzyme or antibody (e.g. paragraphs [0168] and [0354]). The system taught by Cheo et al is capable of stable and random insertion into discrete genomic positions in a host cell, where the expression levels of the first reporter gene inserted at a first site and the expression levels of a second reporter gene inserted at a second site are capable of being selected for quantitatively equivalent expression levels.

Regarding claim 90, Cheo et al teach the expression system, wherein the reporter genes encode cell surface proteins that are membrane-bound proteins (paragraph [0258]).

Regarding claim 92, Cheo et al teach the expression system, wherein the multisubunit complex is an antibody (e.g. paragraph [0168]).

Regarding claims 93 and 94, Cheo et al teach the expression system, wherein the target cassettes contain sequences of antibody light chains and antibody heavy chains (e.g., paragraph [0158]).

Regarding claim 98, Cheo et al teach the use of a first integration cassette comprising a gene encoding a fusion protein comprising an N- or C-terminal tag such as an epitope tag or a six histidine tag (e.g. paragraphs [0062] and [0140]-[0141]).

Regarding claim 99, Cheo et al teach the use of a first integration cassette comprising two, three, four etc. open reading frames that further comprise sequences that function as internal ribosome entry sites (IRES) (e.g. paragraph [0147]). The IRES allows the expression of two structural genes from a single transcript (i.e. bi-cistronic element) (e.g. paragraph [0544]).

Regarding claim 100, Cheo et al teach the use of a first target cassette comprising a gene encoding a fusion protein comprising an N- or C-terminal tag such as an epitope tag or a six histidine tag (e.g. paragraphs [0140], [0141] and [0163]).

Regarding claims 101 and 102, Cheo et al teach the system where each vector contains a selectable marker (e.g., paragraph [0050]).

Regarding claim 103, Cheo et al teach the use of mammalian cells, yeast cells and bacterial cells (e.g. paragraph [0436]). Thus, the integration cassette would be capable of integrating in mammalian, yeast or bacterial cells.

Cheo et al do not teach a rec element encoding at least one flp recombinase activity that recognizes the recombinase recognition sites of the first integration cassette and second integration cassette, where the rec element is included in a separate vector.

Seibler et al teach a rec element, plasmid pOG44, encoding flp recombinase activity (e.g. page 1741, *(d) Recombination Prior to Integration*). Seibler et al teach a first integration cassette, a first target cassette and a rec element. Seibler et al teach a first integration cassette (P construct) comprising an FRT site interposed between an SV40 promoter and a bicistronic

expression unit consisting of the SEAP and HygTk genes followed by a second FRT site different from the first FRT site (e.g. Figure 2; paragraph bridging pages 1742-1743). The first integration cassette is capable of random integration into the genome of a cell (e.g. page 1741, *Transfection (Stable Expression)*). Seibler et al teach a first target cassette (promoter-free exchange plasmid) comprising a bicistronic expression unit, consisting of the luciferase and puromycin resistance genes, flanked by FRT sites capable of recombining with the first and second FRT sites of the first integration vector (e.g. Figure 2; paragraph bridging pages 1742-1743). Seibler et al teach the use of an Flp recombinase activity in mammalian cells (e.g. Table 1; Figure 1; page 1741, *(d) Recombination Prior to Integration*; Figure 3). Seibler et al teach that mammalian cells are capable of supporting recombinase mediated cassette exchange (RMCE), which will provide advantages including the ability to create reference integration sites characterized by their expression potential and long-term stability (e.g. page 1747, left column).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Cheo et al with regard to the cellular expression system capable of performing site-specific recombinase mediated cassette exchange to include the rec element encoding flp recombinase taught by Seibler et al because Cheo et al teach it is within the ordinary skill in the art to perform recombination reactions *in vivo* in mammalian cells and Seibler et al teach the use of flp recombinase activity encoded by a plasmid to mediate site-specific recombination reactions *in vivo* in mammalian cells.

One would have been motivated to make such a modification in order to receive the expected benefit of identifying reference integration sites in the mammalian genome for reproducible levels of expression as taught by Seibler et al. Based upon the teachings of the

cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 91 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cheo et al (US Patent Application Publication No. 2002/0007051, cited in a prior action; see the entire reference) in view of Seibler et al (Biochemistry, Vol. 36, pages 1740-1747, 1997, cited in a prior action; see the entire reference) as applied to claims 89, 90, 92-95 and 97-103 above, and further in view of Ogilvy et al (Blood, Vol. 94, No. 6, pages 1855-1863, 1999, cited in a prior action; see the entire reference). This is a new rejection, necessitated by the addition of new claim 91 in the reply filed 9/17/2007.

The combined teachings of Cheo et al and Seibler et al are described above and applied as before.

Cheo et al and Seibler et al do not teach the expression system, wherein the reporter gene encodes CD4.

Ogilvy et al teach an hCD4 reporter to facilitate mammalian cell-by-cell analysis (e.g., by flow cytometry) (e.g. page 1855, Materials and Methods; page 1857, left column, 1st full paragraph; Fig 1D and E). Ogilvy et al teach that the CD4 reporter was chosen because its molecular interactions have been well characterized and monoclonal antibodies are available that recognize it specifically (e.g. page 1857, left column 1st full paragraph). Ogilvy et al teach the reporter cassette bound by FRT sites to provide the option of Flp-mediated recombination to aid in replacing the hCD4 reporter by another gene.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the hCD4 reporter taught by Ogilvy et al in the integration cassettes of Cheo et al, because Cheo et al teach the inclusion of phenotypic markers such as cell surface proteins, and Ogilvy et al teach the use of hCD4 as a cell surface reporter in a cassette flanked by FRT recombination sites.

One would have been motivated to use the hCD4 reporter of Ogilvy et al because it allows cell-by-cell analysis, its molecular interactions have been well characterized, and monoclonal antibodies are available that recognize it specifically. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 91 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cheo et al (US Patent Application Publication No. 2002/0007051, cited in a prior action; see the entire reference) in view of Seibler et al (Biochemistry, Vol. 36, pages 1740-1747, 1997, cited in a prior action; see the entire reference) as applied to claims 89, 90, 92-95 and 97-103 above, and further in view of Mazda et al (Journal of Immunological Methods, Vol. 169, pages 53-61, 1994, cited in a prior action; see the entire reference. This is a new rejection, necessitated by the addition of new claim 91 in the reply filed 9/17/2007.

The combined teachings of Cheo et al and Seibler et al are described above and applied as before.

Cheo et al and Seibler et al do not teach the expression system, wherein the reporter gene encodes CD8.

Mazda et al teach nucleic acid constructs comprising the murine CD8α gene cDNA, which is used as a reporter/marker gene (e.g. Abstract; Figure 1). Mazda et al teach that the advantages of using CD8 as a reporter or marker is that the assay for CD8 expression is rapid and easy to perform—cell lysates do not need to be prepared and radioisotopes are not required (e.g. paragraph bridging pages 59-60). Further, the use of CD8 allows other reporter and control genes to analyzed simultaneously if desired (e.g. paragraph bridging pages 59-60). CD8 expression can be analyzed at the single cell level, while the cell remains viable, and the expression is highly reproducible (e.g. page 60).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the CD8 reporter taught by Mazda et al in the integration cassettes of Cheo et al, because Cheo et al teach the inclusion of phenotypic markers such as cell surface proteins, and Mazda et al teach the use of murine CD8 as a cell surface reporter.

One would have been motivated to use the CD8 reporter of Mazda et al because it allows cell-by-cell analysis, while the cells remain viable, and the assay is rapid and easy to perform. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim 96 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cheo et al (US Patent Application Publication No. 2002/0007051, cited in a prior action; see the entire

reference) in view of Seibler et al (Biochemistry, Vol. 36, pages 1740-1747, 1997, cited in a prior action; see the entire reference) as applied to claims 89, 90, 92-95 and 97-103 above, and further in view of Ow (US Patent Application Publication No. 2002/0123145, cited in a prior action; see the entire reference). This is a new rejection, necessitated by the addition of new claim 96 in the reply filed 9/17/2007.

The combined teachings of Cheo et al and Seibler et al are described above and applied as before.

Cheo et al and Seibler et al do not teach the inclusion of the rec element in the first and/or second target cassette.

Ow teaches a first integration cassette, first target cassette and rec element. Ow teaches a first integration cassette (receptor construct) comprising a promoter operably linked to a first exchangeable reporter segment comprising a thymidine kinase (tk) coding region and a zeocin resistance coding region, wherein the tk coding sequence is linked to a first recombinase recognition site (PP') at its 5' end and to a second recombinase recognition site at its 3' end (PP') (e.g. Figure 4). More generally, Ow teaches integration cassettes comprising a polynucleotide flanked by two irreversible recombination sites (IRSs), which are stably integrated into the genome of a host organism (e.g. paragraphs [0014] and [0042]). Because the cassettes do not comprise sequence homologous to a chromosome of the target organism, integration will be random. Ow teaches a first target cassette (donor construct) comprising a third recombinase recognition site (BB'), capable of recognizing the first recognition site in the first integration cassette; a first target element (cDNA); and a fourth recombinase recognition site (BB'), capable of recognizing the second recombinase recognition site in the first integration cassette (e.g.

Figure 4). More generally, Ow teaches target cassettes comprising a polynucleotide flanked by two irreversible complementary recombination sites (CIRSs) (e.g. paragraphs [0014] and [0042]). Ow teaches a rec element encoding a recombinase polypeptide capable of catalyzing a recombination reaction between IRS and CIRS, wherein introduction of the rec element and the first target cassette to the recombinant cell population comprising the first integration cassette results in site-specific substitution of the first exchangeable reporter segment with the first exchangeable target segment (e.g. Figure 4, paragraphs [0014], [0037] and [0054]). Ow teaches that the rec element (polynucleotide encoding the recombinase) can be included in the first integration cassette (receptor construct) containing the IRSs (e.g. paragraphs [0045] and [0054]). Ow teaches that the rec element can be included in the first target cassette (donor construct) containing the CIRSs (e.g. paragraph [0054]). Ow teaches the use of the abovementioned system in host cells such as mammalian cells, fungi and bacteria.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include the rec element in the first and/or second target cassette, because Cheo et al and Ow et al teach is it within the skill of the art to use recombinase activity to perform site specific recombination and exchange of nucleic acid segments and Seibler et al teach a vector encoding the rec element.

One would have been motivated to include the rec element in either the target cassettes of Cheo et al in order to receive the expected benefit of having a system where fewer nucleic acid molecules need to be introduced into the cell in order to support the desired recombination method. Based upon the teachings of the cited references, the high skill of one of ordinary skill

in the art, and absent any evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Response to Arguments - 35 USC § 103

The rejection of claims 66 and 69-88 under 35 U.S.C. 103(a) as being unpatentable over Cheo et al in view of Seibler et al and Mazda et al is moot in view of Applicant's cancellation of the claims in the reply filed 9/17/2007.

The rejection of claims 66-88 under 35 U.S.C. 103(a) as being unpatentable over Cheo et al in view of Seibler et al, Ow, and Mazda et al is moot in view of Applicant's cancellation of the claims in the reply filed 9/17/2007.

Applicant's arguments filed 9/17/2007 have been fully considered with respect to the new rejections presented above but they are not persuasive.

The response asserts that the combination of Cheo et al, Seibler et al and Mazda et al fail to teach or suggest all of the limitations recited in amended claim 89. Specifically, the response asserts that Cheo et al do not teach site specific recombination between an exchangeable reporter segment located in a discrete genomic location and a target cassette located in an episomal vector. The response also asserts that Cheo does not teach or suggest site-specific recombination of two nucleic acid sequences encoding two subunits of a multisubunit protein into two discrete and separate genomic positions. Further, the response asserts that Seibler et al do not teach an expression system to express multisubunit proteins and do not cure the deficiency of Cheo et al. Moreover, the response asserts that Mazda et al do not cure the deficiency of Cheo et al.

This is not found persuasive because Cheo et al teach integration cassettes and target cassettes that meet each of the structural limitations of the rejected claims. The vectors taught by Cheo et al are capable of stable, random integration into more than one discrete position in the genome. One would be capable of screening these integration sites for equivalent levels of expression from a first and second integration vector. Thus, the integration and target cassettes taught by Cheo et al meet all of the structural and functional limitations of the claims. The claims are limited to the products of the expression system and are not drawn to a method of using the expression system. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., method steps requiring recombination between a genomic site and an episome or recombination at two discrete and separate genomic positions) are not limitations of the rejected claim(s). In the instant case, the claims are drawn to a product not a process. The claims require the product to be capable of stable and random insertion into discrete genomic positions in a host cell and must be capable of producing quantitatively equivalent expression of the reporters of the first and second integration cassette. The present specification teaches that the integration cassettes are integrated randomly into the genome and screened for the desired expression level (e.g., paragraph [16]). The integration cassettes of Cheo et al are capable of random insertion into a discrete site in the genome, and one could screen for a desired expression level of the reporter. If a prior art structure is capable of performing the intended use, then it meets the limitations of the claim. See, e.g., *In re Schreiber*, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997). Accordingly, Cheo et al teach the claimed integration and target cassettes, and Seibler et al and Mazda et al are not specifically relied upon for these structures.

The response asserts that the combination of Cheo et al, Seibler et al, Ow, and Mazda et al fail to teach or suggest all of the limitations recited in amended claim 89. Specifically, the response asserts that Ow does not teach or suggest site-specific recombination of two nucleic acid sequences encoding two subunits of a multisubunit protein into two discrete and separate genomic positions. This is not found persuasive, because Cheo et al teach the claimed integration and target cassettes, and thus Ow is not specifically relied upon for these limitations. As discussed above, the claims are drawn to products and not methods. The products taught by Cheo et al are capable of performing the recited functions and thus meet the limitations of the claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached at 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

/JD/

/Daniel M. Sullivan/
Primary Examiner
Art Unit 1636